

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1.- 4. (Cancelled)

5. (Currently Amended) A mixture comprising a crystalline biological target molecule and a plurality of core fragments selected from a library of claim 4 of core fragments, wherein at least 40% of the plurality of core fragments comprise an anomalous dispersion substituent.

6. - 49. (Cancelled)

50. A method of designing a lead candidate having biophysical or biochemical activity against a biological target molecule, comprising

a) Combining a crystalline biological target molecule with a mixture comprising at least two compounds, wherein at least one of said compounds comprises a substituent having anomalous dispersion properties;

b) ~~Identifying a compound bound to said biological target molecule~~
Determining the structure of at least one of said compounds in association with said biological target molecule using x-ray crystallographic analysis; and

c) ~~Synthesizing a lead candidate molecule comprising the step of replacing said anomalous dispersion substituent with a substituent comprising a functionalized carbon, nitrogen, oxygen, or sulfur atom;~~ Selecting information from the structure to design said lead candidate

d) ~~Assaying said lead candidate molecule for biophysical or biochemical activity against said biological target molecule.~~

51. - 56. (Cancelled)

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57. (New) The method of claim 50, wherein said identifying of said compound of step b uses the anomalous dispersion properties of said substituent.

58. (New) The mixture of claim 4, wherein about half of said core fragments in said mixture comprise an anomalous dispersions substituent.

59. (New) The mixture of claim 4, wherein said plurality of core fragments comprises at least 10 core fragments.

60. (New) The mixture of claim 4, wherein said anomalous dispersion substituent is bromine.

61. (New) The method of claim 56, wherein said selecting information comprises selecting computed deformation energy of binding information, volume overlap information, induced fit information, computed electrostatic interaction information, and/or computed binding free energy information.

62. (New) The method of claim 56, wherein said selecting information comprises selecting computed energy minimization energy and/or computed molecular dynamics information.

63. (New) The method of claim 56, wherein said substituent is bromine.

64. (New) A method of identifying a core fragment comprising an anomalous dispersion substituent, said core fragment bound to a crystalline biological target molecule, wherein said identifying of said core fragment uses the anomalous dispersion properties of said anomalous dispersion substituent.

65. (New) The method of claim 64, wherein said core fragment forms part of a library of core fragment compounds

66. (New) The method of claim 64, wherein said anomalous dispersion substituent is bromine

67. (New) A method of screening a plurality of core fragments for a core fragment that binds to a biological target molecule, wherein at least one of said compounds comprises a substituent having anomalous dispersion properties, said method comprises the steps of:

- a. soaking a crystal comprising the biological target molecule in a solution comprising said plurality of core fragments; and
- b. identifying a compound bound to said biological target molecule using x-ray crystallographic analysis.

68. (New) The method of claim 67, wherein said substituent is bromine.

69. (New) The method of claim 67, wherein said identifying of said compound of step b uses the anomalous dispersion properties of said substituent.